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Hypertension guidelines – is it time to reappraise blood pressure thresholds and targets?

Rhian M Touyz MD, PhD, and Anna F Dominiczak MD

Institute of Cardiovascular and Medical Sciences, British Heart Foundation (BHF)

Glasgow Cardiovascular Research Centre, University of Glasgow, UK.

Short title: Blood pressure targets and hypertension guidelines

Correspondence

Rhian M Touyz, MD, PhD and Anna F. Dominiczak MD

Institute of Cardiovascular and Medical Sciences,

BHF Glasgow Cardiovascular Research Centre,

College of Medical, Veterinary and Life Sciences,

University of Glasgow,

126 University Place, Glasgow, G12 8TA

Phone: + 44 (0)141 330 7775/7774; Fax: + 44 (0)141330-3360,

Email: Rhian.Touyz@glasgow.ac.uk; Anna.Dominiczak@glasgow.ac.uk

Heart disease, stroke and renal failure are leading causes of death with hypertension being the predominant risk factor (1,2). Extensive evidence from randomized controlled trials has clearly demonstrated benefit of antihypertensive treatment and blood pressure reduction in reducing cardiovascular events in individuals with hypertension (3-5). Accordingly effective blood pressure control is essential to prevent the adverse sequelae of hypertension. While modern drugs have the capacity to reduce blood pressure in almost every patient with hypertension (6,7), the actual blood pressure thresholds at which treatment should be initiated and the target levels at which blood pressure should be maintained still remain a topic of much discussion and debate.

To inform health care providers and to provide pragmatic clinical suggestions and recommendations, international, regional and national hypertension guidelines have been developed by expert groups globally. Most major hypertension treatment guidelines currently suggest that clinicians should strive to treat adults to a blood pressure target of d140/90 mmHg (8-14). Regarding goals for older individuals, a 2014 report from panel members of the eighth joint national committee (JNC8) suggested that in persons aged 60 years or older blood pressure should be targeted to less than 150/90 mmHg (12). The French guidelines recommend that individuals 80 years or older should be treated to a target of 150/90 mmHg (15), while the Canadian guidelines suggest that in the very elderly (e 80 years) the threshold for initiating drug treatment should be 160 mmHg (14).

Hypertension guidelines, in large part, are evidence-based and are usually dictated by randomized controlled trial data and observational studies. While there is general consensus between major guidelines that treatment should aim at lowering blood pressure in adults to 140/90 mmHg (8-14), what has been less clear is whether there is

further cardiovascular benefit when blood pressure is treated more intensively to a goal lower than 140/90 mmHg.

Exactly how low blood pressure should be targeted remains a matter of intense discussion. This is highlighted by the many studies that have demonstrated that below a certain level of blood pressure, more aggressive reductions may not be associated with benefit and actually increase the risk of harm. The notion of the 'J-curve' defined as the occurrence of additional cardiovascular events when the blood pressure is lowered beyond the level required to maintain tissue perfusion, refers primarily to diastolic blood pressure (16,17). Exactly what the critical diastolic blood pressure is, particularly in the population at large, is still unclear but treatment to a level below 65mmHg has been suggested to be associated with additional harm (16-18). Current guidelines suggest treatment targets for diastolic blood pressure below 90 mmHg, which seems 'safe' in the J-curve phenomenon.

But what about systolic blood pressure? Is there a J-curve for systolic blood pressure and is 140 mmHg truly the level associated with maximum benefit? Despite guidelines suggesting this, until recently, there was little evidence that lower systolic blood pressure targets may have greater cardiovascular protection. However, three recent important studies, SPRINT (19) and two large meta-analyses clearly showed that lower systolic blood pressures may indeed be better (20,21). The main finding in SPRINT was that a primary composite outcome of cardiovascular disease and death was reduced by 25% and all-cause mortality by 27% in patients treated intensively to a systolic blood pressure target of <120 mmHg (19). However, it should be stressed that SPRINT was restricted to hypertensive adults, including the eldery (> 75 years), at above-average risk of cardiovascular disease and that diabetic patients and those who had already had a stroke, were excluded (12). Xie et al (20), in a meta-analysis of

over 44,000 patients, showed that intensive blood pressure lowering below 140 mmHg was associated with improved cardiovascular and renal outcomes. Ettehad et al (21) reported in a systematic review and meta-analysis of over 613,000 participants that lowering blood pressure to a systolic blood pressure of less than 130 mmHg significantly reduced cardiovascular events and mortality.

While these recent meta-analyses, together with the SPRINT findings, are highly suggestive that there is increased benefit when patients with hypertension are treated to systolic blood pressures below the currently suggested target of 140 mmHg, there are some important aspects of these studies that should be highlighted. In particular, the meta-analyses comprised trials with heterogeneous cohorts and thus identifying those individuals who would benefit most from intensive treatment to lower blood pressure targets is difficult. In addition, in all three studies, the focus of intensive therapy was on systolic blood pressure and it remains unclear whether a concomitant reduction in diastolic blood pressure (which is likely with intensive anti-hypertensive treatment), would also result in a reduced rate of cardiovascular events. Not with standing some of these issues the potential impact of SPRINT and the recent meta-analyses, on diagnosing, treating and managing patients with hypertension is immense, not only from the health-care and patients well-being point of view, but also from the societal and health economic position. It is likely that these studies will lead to changes in clinical practice. Accordingly, it is now timely to re-think blood pressure thresholds and targets. As hypertension experts we have the responsibility to re-evaluate current evidence and re-appraise guidelines for diagnosis and management. Exactly what the future recommendations will be remain uncertain, because the data from the recent studies (19-21) still need to be digested and further analysed in the context of current evidence-based studies, but it is very likely that

there will be a strong move towards more aggressive control of hypertension to lower blood pressure targets. With the awaited new ACC/AHA guidelines soon to be finalized, re-assessment of existing guidelines and more SPRINT sub-studies to be published, the landscape of diagnosing and treating hypertension may change significantly in the near future.

Over the next few months, we will seek opinions and comments from key leaders involved in regional and international hypertension guidelines. As such we will provide views from across the world regarding the potential impact of the new findings of lower systolic blood pressure targets and future guidelines. Through this platform, 'Hypertension', as the premier journal in the field, will serve the hypertension community by keeping readers abreast of how the new land-mark studies will influence major guidelines and decision-making for best practice.

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